

AMENDMENT

A listing of the claims presented in this patent application appears below. This listing replaces all prior versions and listing of claims in this patent application.

Claim 1 (currently amended): A method of identifying a compound which modulates binding of a natural ligand to the EGF receptor, ErbB3 or ErbB4, or which modulates signal transduction ~~via by binding to~~ the EGF receptor, ErbB2, ErbB3 or ErbB4, which method comprises the steps of:

(A) assessing the stereochemical complementarity between the compound and ~~the a~~ molecule, wherein the molecule comprises:

(i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations; or

(iii) amino acids present in the amino acid sequence of ErbB2, ErbB3 or ErbB4, which form an equivalent three-dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(B) ~~obtaining selecting~~ a compound assessed in step (A) which possesses stereochemical complementarity to the molecule;

(C) testing the compound in vivo or in vitro for its ability to

(i) modulate binding of a natural ligand to the EGF receptor, ErbB3 or ErbB4, or

(ii) modulate signal transduction ~~via by binding to~~ the EGF receptor, ErbB2, ErbB3 or ErbB4; and

(D) selecting and obtaining a compound tested in step (C) that has the ability to

(i) modulate binding of a natural ligand to the EGF receptor, ErbB3 or ErbB4, or

(ii) modulate signal transduction by binding to the EGF receptor, ErbB2, ErbB3 or ErbB4.

Claims 2 - 53 (canceled).

Claim 54 (original): The method according to claim 1, wherein the testing in (C) is carried out *in vitro*.

Claim 55 (original): The method according to claim 54, wherein the testing is performed by a high throughput assay.

Claim 56 (original): The method according to claim 1, wherein the testing in (C) is carried out *in vivo*.

Claim 57 (original): The method of claim 1, in which step (C) (ii) involves testing the compound for the ability to modulate EGF receptor, ErbB2, ErbB3 or ErbB4 mediated cell proliferation.

Claim 58 (currently amended): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) is defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

Claim 59 (currently amended): The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent three-dimensional structure to that of the region defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

Claim 60 (currently amended): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) is defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

Claim 61 (currently amended): The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent three-dimensional structure to that of the region defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

Claim 62 (canceled).

Claim 63 (original): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) are the amino acids that form the β -sheet of the L1 domain of the EGF receptor.

Claim 64 (currently amended): The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent ~~three-dimensional~~ three-dimensional structure to that of the β -sheet of the L1 domain of the EGF receptor.

Claim 65 (original): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) are the amino acids that form the β -sheet of the L2 domain of the EGF receptor.

Claim 66 (currently amended): The method of claim 1, wherein the amino acids in step (A)(iii) are present in the amino acid sequence of ErbB2, ErbB3 or ErbB4 and form an equivalent ~~three-dimensional~~ three-dimensional structure to that of the β -sheet of the L2 domain of the EGF receptor.

Claim 67 (currently amended): The method of claim 1, which further includes the step of modifying the compound selected in step (B) or step (D) such that to enhance binding to a lower face containing the second β -sheet of the L1 and/or L2 domains is enhanced in the modified compound compared to the unmodified compound, wherein the structure of the face is characterized by a plurality of solvent-exposed hydrophobic residues.

Claim 68 (original): The method of claim 67, in which the hydrophobic residues include:

- (i) Tyr64, Leu66, Tyr89, Tyr93; and/or
- (ii) Leu348, Phe380 and Phe412.

Claim 69 (original): The method of claim 1 in which the compound is identified from test compounds in a database.

Claim 70 (currently amended): The method of claim 1, which further includes the step of selecting a compound that increases signal transduction via by binding to the EGF receptor, ErbB2, ErbB3 or ErbB4.

Claim 71 (currently amended): The method of claim 1, which further includes the step of selecting a compound that decreases signal transduction via by binding to the EGF receptor, ErbB2, ErbB3 or ErbB4.

Claim 72 (original): The method of claim 1, which further includes the step of selecting a compound that inhibits or prevents the binding of a natural ligand to the EGF receptor, ErbB3 or ErbB4.

Claim 73 (currently amended): A method of identifying a compound which binds to a molecule of the EGF receptor family selected from the group consisting of the EGF receptor, ErbB2, ErbB3 and ErbB4, which method comprises the steps of:

(A) assessing the stereochemical complementarity between the compound and the molecule, wherein the molecule comprises:

- (i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;
- (ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations; or
- (iii) amino acids present in the amino acid sequence of ErbB2, ErbB3 or ErbB4, which form an equivalent three-dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;

(B) ~~obtaining one or more compounds which possesses stereochemical complementarity to the molecule selecting a compound assessed in step (A) which possesses stereochemical complementarity to the molecule; and~~

(C) ~~selecting a compound from step B that has an experimentally determined K_d or K_I of less than 10⁻⁶ M for a molecule of the EGF receptor family selected from the group consisting of the EGF receptor, ErbB2, ErbB3 and or ErbB4.~~

Claim 74 (original): A method as claimed in claim 73, wherein K_d is less than 10⁻⁸M.

Claim 75 (original): The method of claim 73, wherein K_I is less than 10⁻⁸M.